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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,707	06/07/2001	Theresa M. Allen	5325-0148.34	1073

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 01/29/2004

18

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/876,707

Applicant(s)

ALLEN ET AL.

Examiner

Gollamudi S Kishore, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 03 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 21-32 and 57-81 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-32 and 57-81 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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### **DETAILED ACTION**

The request for the extension of time and amendment dated 10-3-04 are acknowledged.

Claims included in the prosecution are 21-32 and 57-81.

#### *Claim Rejections - 35 U.S.C. ' 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 21-32 and 57-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Torchilin (\*5,534,241) in view of Harris (5,932,462).

Torchilin as pointed out before, discloses a polymer system (DTPA-polylysine) one end of which is attached to a lipid and the other to either a therapeutic or diagnostic polychelator (targeting ligand); (note the abstract, figures, columns 4-5, 9-13

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and claims). Torchilin also teaches the use of other targeting groups such as enzymes, lectins and antibodies in the liposomes compositions and protective polymers such as PEG (same polymer as in instant invention) on col. 2, lines 18-59 and col. 9, 34-48.

Torchilin does not specifically teach that these ligands could be attached to the polymer via the activated groups instead of the polychelating ions, or in addition to the polychelating agent or on the protective polymer, PEG.

Harris while disclosing a multi-armed polymer systems containing PEG-lysine polymers teaches that the polymer functional groups could be activated to couple to various target ligands (columns 12, 26, 36, 37 and claims).

It would have been obvious to one of ordinary skill in the art to use any targeting molecule in the polymer complex of Torchilin with the expectation of obtaining at least similar results since Harris teaches that any ligand could be coupled to the hydrophilic polymer system.

Applicant=s arguments have been fully considered, but are not found to be persuasive. Applicant argues that Torchilin describes a lipid-polymer –polychelating agent, where the polychelating agent has no binding affinity for a receptor expressed on a cell. This argument is not found to be persuasive since Torchilin’s invention concerns with both therapeutic and diagnostic purposes and on col. 12, lines 6-10 Torchilin teaches that the liposomes are additionally modified with a target group and or other surface modifications. Torchilin also teaches the attachment of antibodies (claim 5)

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These are suggestive of the use of any group, which could serve as the targeting ligand including those which recognize receptors on the cell surface. Torchilin's intent of attaching other targeting moieties is also clear from his teachings on col. 2, lines 18-59.

Applicant's arguments that it does not make sense to modify Torchilin according to the teachings of Harris since Harris describes a multi-armed monofunctional polymer having a single reactive site (moiety Z in the structure of the abstract and claim 1). Furthermore, according to applicant, the single reactive site means that the polymer cannot be a link between lipid and a polymer, as needed to combine with Torchilin to arrive at the present invention. This argument is not found to be persuasive: first of all, Harris is combined for its teachings of various targeting ligands. This would be the same irrespective of the number of reactive sites in Harris's polymer. Secondly, as pointed out before, although Harris is directed to a polymer ligand combination, on col. 2, line 45 through col. 3. Line 20 the reference clearly teaches that polyethylene glycol (same as in instant invention) has two functional hydroxyl groups and both could be activated to react with amino groups and Harris is clearly indicative of the attachment of targeting ligands to one of the activated groups. The primary reference of Torchilin as discussed above and as recognized by applicants themselves, teaches the attachment of polyethylene glycol to the liposome surface via amino linkages on the phospholipid head group (note also col. 10, lines 15-55) and Torchilin also provides guidance to attach one end of the polymer chain to the liposomal surface and the other to the

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chelating ligand. It is therefore, would have been obvious to one of ordinary skill in the art from the combined teachings of Torchilin and Harris to couple a targeting ligand and the liposomal surface to PEG with a reasonable expectation of success.

As pointed out before, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, although Harris is directed to a polymer ligand combination, on col. 2, line 45 through col. 3. Line 20 the reference clearly teaches that polyethylene glycol (same as in instant invention) has two functional hydroxyl groups and both could be activated to react with amino groups and Harris is clearly indicative of the attachment of targeting ligands to one of the activated groups. The primary reference of Torchilin as discussed above and as recognized by applicants themselves, teaches the attachment of polyethylene glycol to the liposome surface via amino linkages on the phospholipid head group (note also col. 10, lines 15-55) and Torchilin also provides guidance to attach one end of the polymer chain to the liposomal surface and the other to the chelating ligand. It is therefore, would have been obvious to one of ordinary skill in the art from the combined teachings of Torchilin and Harris to couple a targeting ligand and the liposomal surface

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to PEG with a reasonable expectation of success. Therefore, applicant's argument that there is no suggestion to combine the references is not found to be persuasive and the rejection is maintained.

3. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703) 308-2927. The fax phone number for this Group is (703) 305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.



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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

A handwritten signature in black ink, appearing to read 'G S Kishore'.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

January 26, 2004